

### **REMARKS**

Claims 1 and 84-115 are pending. Applicants respectfully request entry of the claim amendments listed above. Claims 1, 89 and 90 have been amended for clarification.

#### **Rejections under 35 USC § 112, second paragraph**

The Examiner has rejected claims 1, 84-100 and 102-115 under 35 USC § 112, second paragraph as being indefinite for failing to particularly point out and distinctly claim the subject matter of the invention. Applicants respectfully traverse this rejection. However, to expedite the prosecution of the subject application, Claim 1 step f) has been amended to clarify the identification of proportional ancestry to at least two ancestral groups and to clarify step (ii) to recite 'correlating population structure with nucleotide occurrences.' Claims 89 and 90 have been amended to recite 'selected from the group consisting of.' Applicants request withdrawal of this objection.

#### **Response to Continued Rejections Under 35 USC § 103(a)**

In response to the continued rejection of claims 1 and 84-115 under 35 U.S.C. § 103(a) for obviousness over Parra *et al.* (2001) Applicant respectfully traverses the Examiners assertions "the prior art's mere disclosure of more than one alternative does not criticize, discredit, or otherwise discourage the solution claimed...." In re Fulton, 391 F.3d 1195, 1201, 73 USPQ2d 1141, 1146 (Fed Cir. 2004) and MPEP § 21223. As previously stated by Applicant, a fundamental aspect of the method disclosed by Parra *et al.* is the prior knowledge and selection of parental populations (Parra *et al.* p. 19 col. 1). Parra *et al.* acknowledges this fundamental requirement and refers to this prior knowledge as a key aspect to his determination of the ancestral proportion of a single ancestry from a known population. Applicants assert that the instant invention discloses a method of identifying the proportional ancestry of at least two ancestral groups from a test subject from whom no prior information is known. Applicants assert that the fundamental element of the method disclosed in Parra *et al.* of a known parental population is not an alternative to the method of the instant

invention but a fundamentally different method that teaches away from the invention of the instant application.

In response to the continued rejection of claims 1, 84-101, and 104-115 are rejected under 35 U.S.C. § 103(a) for obviousness over Parra *et al.* (2001) Am. J. Physical Antropol. Vol. 114(1):18-29, Cargill *et al.* (1999) Nature Genetics Vol. 22:231-238, and Shriver *et al.* (1997) American Journal of Human Genetics Vol. 60:957-964. Applicants respectfully traverse the Examiner's assertions that the claims of the instant invention do not teach large numbers of samples for determining BGA proportions, the claims do not recite any limitations directed to testing a particular size of a patient population, nor any specific limitation regarding a "large" number of samples. Applicants respectfully disagree. Claim 1 requires an *in silico* database to identify a first population of SNPs. *In silico* SNP databases by their very nature are large. For example, as of filing date of the instant application the NCBI SNP database contained more than 9 million identified human SNPs (NCBI build 116 released August 7, 2003). Applicants assert that by requiring the *in silico* SNP database in Claim 1 step a), the claims of the instant invention do contain teachings and limitations regarding a 'large' number of samples.

In response to Examiner's assertion that unexpected results must be established by factual evidence based on MPEP Section 716.01(c). Applicants respectfully traverse the Examiners statements that there is no data comparing Applicants method with those of the closet prior art, Parra *et al.*, showing an unexpected advantage and that due to the lack of such tests Applicants assertion of unexpected results is mere argument. Applicants assert that the method disclosed by Parra *et al.* and the method disclosed in the instant application are fundamentally different and cannot be compared fairly side by side. As previously discussed, Parra *et al.* does not disclose a method for inferring the proportional ancestry for at least 2 ancestral groups of a test subject, but rather a method for determining the ancestral proportion for a single ancestry from a known and defined population. As such, no comparison can be made. Applicants assert that the data shown in Example 2 provides evidence that the instant invention exceeds one skilled in the art's reasonable expectation of success. As stated in Example 2:

‘Because a large number of high  $\delta$  value markers were used, the test was **surprisingly robust**; reasonable levels of simulated allele frequency errors that could be caused by biased parental sampling had no significant impact on the BGA proportions determined.’ (emphasis added).

Applicants assert that the method disclosed in the instant application has exceeded the reasonable expectations of one skilled in the art for determining proportional ancestry for at least two ancestral groups in a test subject.

**First Rejection under 35 USC § 103(a)**

A claimed invention may be invalid if it is obvious in view of a combination of elements taken from the prior art: “A combination of familiar elements according to known methods is likely to be obvious when it does no more than yield predictable results.” *KSR Intern. Co. v. Teleflex Inc.*, 550 U.S. 398, 416 (2007). To ascertain whether an invention is obvious, a set of factors known as the “Graham factors” originally set out by the Supreme Court in *Graham v. John Deere Co.*, 383 U.S. 1, 17 (1966) are considered: (1) the scope and content of the prior art, (2) the differences between the claimed invention and the prior art, (3) the level of ordinary skill in the art, and (4) any secondary considerations such as commercial success or long-felt but unsolved need.

“*Graham* is interpreted as continuing to place the ‘burden of proof on the Patent Office which requires it to product the factual basis for its rejection of an application under sections 102 and 103.’” *In re Piasecki*, 745 F.2d 1468, 1472 (Fed. Cir. 1984). A *prima facie* case is typically established by a motivation to combine the references and a reasonable expectation of success to one of ordinary skill in the art. “Where claimed subject matter has been rejected as obvious in view of a combination of prior-art references, a proper analysis under 35 U.S.C. § 103 requires, *inter alia*, consideration of two factors: (1) whether the prior art would have suggested to those of ordinary skill in the art that they should make the claimed composition or device, or carry out the claimed process; and (2) whether the prior art would also have revealed that, in so making or

carrying out, those of ordinary skill would have a reasonable expectation of success. Both the suggestion and the reasonable expectation of success must be founded in the prior art, not in the applicant's disclosure." *In re Vaeck*, 947 F.2d 488, 493 (Fed. Cir. 1991).

The Examiner has rejected claims 1, 84-86, 91-96, 98-100 and 104-109 as being unpatentable over Parra *et al.* (Am. J. Physical Anthropol., January 2001, Vol. 114, Issue 1, p. 18-29), in view of Cargill *et al.* (Nature Genetics, 1999, Vol. 22, p.231-238) and in view of Shriver *et al.* (Am. J. Hum. Genetics, 1997, Vol. 60, p. 957-964). Applicants respectfully traverse this rejection.

As discussed previously and above, Parra *et al.* does not disclose a method for inferring the proportional ancestry of at least two ancestral groups of a test subject, rather Parra *et al.* discloses a method to determine the ancestry proportion of a single ancestry from a known and defined population. These are fundamentally two very different methods with very different objectives. The instant invention provides a method for determining what the ancestral make up of a test subject is, while the method disclosed in Parra *et al.* merely confirms the presence of an ancestral group from a known population. In fact, as stated above Parra *et al.* teaches away from the instant application.

Additionally, as noted by the Examiner, Parra *et al.* does not disclose the statistical methods of the instant application (i.e. six 2-way, three 3-way or one 4-way comparisons between ancestral groups); a first population of SNPs identified from a database *in silico*; the use of a first population to generate a second population of SNPs wherein at least one SNP of the second population of SNPs have minor allele frequencies of 0.1% and are not located within a region of a gene encoding a protein; performing a likelihood determination of proportional affiliations among four ancestral groups having the greatest likelihood values, or performing a likelihood determination for affiliation with an East Asian ancestral group.

The Examiner states that Cargill *et al.* discloses a method for screening samples to determine whether identified SNPs are coding or noncoding SNPs. The Examiner further states that

Shriver *et al.* discloses a method for determining ethnic affiliations using genetic likelihood analysis. Applicants assert that the disclosures of Cargill *et al.* and Shriver *et al.* fail to correct the multiple deficiencies found in Parra *et al.*

Applicants submit that the Examiner has not established a *prima facie* case of obviousness based on the asserted combination of references, because those skilled in the art would not have been motivated to combine as asserted by the Examiner, and there cannot be a reasonable expectation of success. Further the claimed invention has unexpected results over the asserted combination of references. Accordingly, withdrawal of the obviousness rejection is respectfully requested.

**Second Rejection under 35 USC § 103(a)**

The Examiner has rejected claims 87-90, 97 and 110-115 as being unpatentable over Parra *et al.* (Am. J. Physical Anthropol., January 2001, Vol. 114, Issue 1, p. 18-29), in view of Cargill *et al.* (Nature Genetics, 1999, Vol. 22, p.231-238) and in view of Shriver *et al.* (Am. J. Hum. Genetics, 1997, Vol. 60, p. 957-964) as applied to 1, 84-86, 91-96, 98-100 and 104-109, above, and further in view of Sorenson *et al.* (US2003/0172065) and in view of the NCBI Database. The Examiner states that it would have been obvious to one skilled in the art to modify the method made obvious by Parra *et al.*, Cargill *et al.* and Shriver *et al.* by using additional data such as a photo of a person from whom the known proportional ancestry was determined with a reasonable expectation of success since the use of ancestral data stored on microfiche and in electronic media was known in the art. The Examiner further states that by contacting the samples with SEQ IDs selected from SEQ ID NOs 1-331 or 1-71 in view of the NCBI database which shows that at least one of these SEQ IDs was known in the art.

Applicants respectfully disagree. Applicants assert that the disclosure in Sorenson *et al.* and the NCBI database do not cure the deficiencies found in the Parra *et al.* reference. Sorenson *et al.* discloses a computer based system for determining relatedness between individuals. This is entirely different from the instant application which is directed at inferring proportional ancestry.

Additionally, applicants submit that the instant invention links SNPs with ancestral groups and that the information contained within the NCBI database does not disclose such a link or even suggest such a link. Applicants assert that just because a SNP has been identified, it doesn't necessarily follow that that SNP can be associated with a specific ancestral group.

As discussed above, the Examiner has not established a *prima facie* case of obviousness based on the combination of Parra *et al.*, Cargill *et al.*, and Shriver *et al.* and the disclosure of the cited references including Parra *et al.* actually teaches away from the claimed invention. Further the claimed invention has unexpected results over the asserted combination. Applicants submit that combination with Sorenson *et al.* and the NCBI database cannot cure the defects of the previous asserted combination, and those skilled in the art would not have been motivated to combine Parra *et al.*, Cargill *et al.*, Sorenson *et al.*, Shriver *et al.* and the NCBI database as asserted by the Examiner. Further there cannot be a reasonable expectation of success for the asserted combination and the claimed invention provides unexpected results over the asserted combination.

Accordingly, withdrawal of the obviousness rejection over the combination of Parra *et al.*, Cargill *et al.*, Sorenson *et al.*, Shriver *et al.*, Sorenson *et al.* and the NCBI database is respectfully requested.

### **Third Rejection under 35 USC § 103(a)**

The Examiner has rejected claims 102-103 as being unpatentable over Parra *et al.* (Am. J. Physical Anthropol., January 2001, Vol. 114, Issue 1, p. 18-29), in view of Cargill *et al.* (Nature Genetics, 1999, Vol. 22, p.231-238) and in view of Shriver *et al.* (Am. J. Hum. Genetics, 1997, Vol. 60, p. 957-964) as applied to 1, 84-86, 91-96, 98-100 and 104-109, above, and further in view of Pritchard *et al.* (Theoretical Population biology, 2001, Vol. 60, p.227-237). The Examiner states that Pritchard *et al.* discloses a method for inferring proportional ancestry of different ancestral groups in a population using a graphical display.

Applicants conclude that the Examiner relies on Prichard only for the features recited in claims 102 and 103. As discussed above, the Examiner has not established a prima facie case of obviousness based on the combination of Parra *et al.*, Cargill *et al.*, and Shriver *et al.* and the disclosure of the cited references including Parra *et al.* actually teaches away from the claimed invention. Further the claimed invention has unexpected results over the asserted combination. Applicants submit that combination with Pritchard *et al.* cannot cure the defects of the previous asserted combination, and those skilled in the art would not have been motivated to combine Parra *et al.*, Cargill *et al.*, Sorenson *et al.*, Shriver *et al.* and Pritchard *et al.* as asserted by the Examiner. Further there cannot be a reasonable expectation of success for the asserted combination and the claimed invention provides unexpected results over the asserted combination.

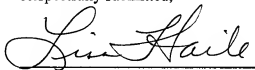
Accordingly, withdrawal of the obviousness rejection over the combination of Parra *et al.*, Cargill *et al.*, Sorenson *et al.*, Shriver *et al.* and Pritchard *et al.* is respectfully requested.

**CONCLUSION**

In view of the above, it is respectfully submitted that Claims 1- 84-100 and 102-115 are allowable over the prior art cited by the Examiner and allowance of these claims and the application is respectfully requested. The Examiner is invited to call Applicant's attorney at the number below in order to speed the prosecution of this application.

The Commissioner is hereby authorized to charge a total amount of \$555.00, which represents payment for a Three Month Extension of Time Fee to Deposit Account No. 07-1896. Additionally, the Commissioner is hereby authorized to charge any fees associated with the filing submitted herewith, or credit any overpayments to Deposit Account No. 07-1896 referencing the above-identified attorney docket number.

Respectfully submitted,



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